DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

OCT _ 7 2002

David M. Fox
Hogan & Hartson, L.L.P.
555 Thirteenth Street, NW
Washington , DC 20004

Re: Docket No. 01P-0560/CP1

Dear Mr. Fox:

This responds to your citizen petition, dated December 11, 2001, and your supplement, dated April 10, 2002, requesting that the Food and Drug Administration (FDA) refrain from approving, under section 505 of the Federal Food, Drug, and Cosmetic Act (the Act), a new drug application (NDA) for any buprenorphine drug product intended for use in the treatment of narcotic addiction prior to:

1. FDA presenting buprenorphine, and the issues involved in its use for the treatment of narcotic addiction, to an advisory committee;

2. FDA preparing a recommendation for the Drug Enforcement Administration (DEA) that buprenorphine be placed in a schedule under the Controlled Substances Act (CSA) more restrictive than Schedule V; and

3. DEA placing buprenorphine in a schedule more restrictive than Schedule V.

We are granting your petition in part and denying it in part for the reasons we set out below.

I. BACKGROUND

Buprenorphine is a derivative of thebaine, a major constituent of opium, presently marketed in the United States as an injectable formulation under the brand name of Buprenex for the treatment of pain. It is classified as a narcotic agonist-antagonist, or partial agonist, with an analgesic potency far greater than morphine (buprenorphine is generally reported to have 20 to 30 times the analgesic potency of morphine sulfate in humans).

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In 1981, FDA approved buprenorphine hydrochloride (HCl) for injection (Buprenex) for marketing under section 505 of the Act (NDA 18-401).[1] In 1985, DEA placed buprenorphine in Schedule V (50 FR 8104), after receiving a recommendation to reschedule prepared by FDA and the Department of Health and Human Services (DHHS) under section 201(d) of the CSA (21 U.S.C. 811(d)). Recently, DEA again proposed rescheduling buprenorphine after receiving another recommendation to reschedule from FDA/DHHS. This proposal was to remove buprenorphine from Schedule V and to place it in Schedule III. The proposal was published and public comments were solicited in the *Federal Register* of March 21, 2002 (67 FR 13114). DEA finalized the proposal and removed buprenorphine from Schedule V and placed it in Schedule III in the *Federal Register* of October 7, 2002 (67 FR 62354).

II. DISCUSSION

A. Advisory Committee

You have asked that FDA present issues regarding the approval of buprenorphine products for the treatment of narcotic addiction to an FDA advisory committee. The question whether to consult an advisory committee regarding issues involved in our review of human prescription drug products is committed solely to FDA's discretion. See 21 CFR 14.171 and 14.172. Furthermore, questions involving the safety and efficacy of buprenorphine and buprenorphine combination products in the treatment of narcotic addiction have already been discussed at two meetings of the former Drug Abuse Advisory Committee (held on April 6, 1995, and February 10, 1997). We do not believe that presenting buprenorphine, and the issues regarding its use for the treatment of narcotic addiction, to an additional advisory committee is warranted before we can act on NDAs for buprenorphine for this indication.

In addition to the input from two advisory committee meetings, the issues surrounding the use of buprenorphine in the treatment of narcotic addiction have been the subjects of many scientific and medical publications. Congress also considered the use of buprenorphine for the treatment of narcotic addiction in its passage of the Drug Addiction Treatment Act of 2000 (Pub. L. 106-310). See 106 H. Rpt. 441; Prt 1. Finally, DEA received several comments on its March 2002 proposal to reschedule buprenorphine, including a comment from you. The use of buprenorphine and buprenorphine combination products for the treatment of narcotic addiction has been the subject of an extraordinary amount of public input and discussion. Under the circumstances, an advisory committee meeting would not be a good use of the Agency's or the committee members' time or resources.[2]

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[1] In addition to Buprenex, we approved Abbott Laboratories' abbreviated new drug application (ANDA 74-137) for buprenorphine HCl for injection in 1996.

[2] We note your claim that we should convene an advisory committee because buprenorphine NDAs have been developed with the support of the National Institute on Drug Abuse (NIDA) (Petition at 8). The implication that NIDA's involvement might influence our review of NDAs is without any basis in fact.

B. Rescheduling Recommendation

You have asked that we complete a recommendation to reschedule buprenorphine to a more restrictive schedule. We have completed an analysis recommending that buprenorphine be placed in Schedule III under the CSA. On December 4, 2001, the Assistant Surgeon General and Acting Principal Deputy Assistant Secretary for Health, DHHS, Arthur J. Lawrence, signed and forwarded to DEA a letter containing that recommendation. A copy of that letter is enclosed. Since drugs listed in Schedule III are subject to more restrictions than those listed in Schedule V, this action complies with your request that we prepare a recommendation for DEA that buprenorphine be placed in a schedule more restrictive than Schedule V. The letter was made available for public inspection and comment as part of DEA's rescheduling procedure. See 67 FR 13114. Accordingly, the portion of your citizen petition requesting that FDA prepare a recommendation for DEA that buprenorphine be placed in a schedule under the CSA more restrictive than Schedule V is granted.

C. Approval of Buprenorphine Drug Products After Rescheduling

You have also asked that FDA refrain from approving any NDAs for buprenorphine for treatment of narcotic addiction before the DEA finalizes the rescheduling of buprenorphine. DEA placed buprenorphine in schedule III on October 7, 2002 (67 FR 62354), prior to our approval of any buprenorphine drug products other than the two products approved prior to the submission of your petition. Accordingly, the portion of your citizen petition requesting that we refrain from approving NDAs for buprenorphine drug products until after DEA had rescheduled buprenorphine is granted.

III. CONCLUSION

For the reasons discussed above, your petition is granted in part and denied it in part. We grant your requests that FDA refrain from approving any buprenorphine drug product (1) before preparing a recommendation for DEA that buprenorphine be placed in a schedule under the CSA more restrictive than Schedule V and (2) until DEA reaches a final scheduling decision. We deny your request that FDA refrain from approving any buprenorphine drug product before presenting buprenorphine, and the issues involved in its use for the treatment of narcotic addiction, to an advisory committee.

Sincerely yours,

Janet Woodcock, M.D.
Director
Center for Drug Evaluation and Research

DEPARTMENT OF HEALTH AND HUMAN SERVICES Office of the Secretary

Assistant Secretary for Health
Office of Public Health and Science
Washington D.C. 20201

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Mr. Asa Hutchinson
Administrator
Drug Enforcement Administration
Washington, D.C. 20537

Dear Mr. Hutchinson:

Pursuant to the Controlled Substances Act (CSA), 21 U.S.C. 811 (b), (c), and (f), the Department of Health and Human Services (DHHS) has conducted a scientific and medical evaluation of buprenorphine. We recommend that buprenorphine be rescheduled from Schedule V to Schedule III of the CSA.

Buprenorphine meets the criteria for placement in Schedule III of the CSA under 21 U.S.C. 812 (b) (3). As discussed in the enclosed analysis, buprenorphine has a potential for abuse less than substances in Schedules I and II, and has a currently accepted medical use in treatment in the United States. Buprenorphine is currently used for the treatment of pain. Abuse of buprenorphine may lead to moderate or low physical dependence or high psychological dependence. Accordingly, DHHS recommends that buprenorphine be subject to control under Schedule III of the CSA.

You will find enclosed the document prepared by the Food and Drug Administration's Controlled Substance Staff that is the basis for the recommendation.

Should you have any questions regarding the recommendation, please contact Corinne P. Moody, Science Policy Analyst, Controlled Substance Staff, at (301) 827-1999.

Sincerely yours,

Arthur J. Lawrence, Ph.D.
Assistant Surgeon General
Acting Principal Deputy Assistant
Secretary for Health

Enclosure